

THE METABOLISM OF CERTAIN AMINO ACIDS
AND THEIR DERIVATIVES

BY
BYRON ELWOOD LEACH

B. S., Mississippi State College, 1938
M. S., Virginia Polytechnic Institute, 1939

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE UNIVERSITY
OF ILLINOIS, 1944

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PART I

GENERAL INTRODUCTION

There are three methods in general use for the study of the nutritive value of amino acids. The first involves the administration of diets in which the sole nitrogen source is supplied in the form of a purified protein, deficient in or devoid of one or more amino acids. The second consists in feeding rations containing hydrolyzed protein from which certain amino acids have been removed as completely as possible. In the third method, mixtures of highly purified amino acids are fed as the sole nitrogen source. The latter method was employed in the following experiments.

PART II

AVAILABILITY OF CERTAIN DERIVATIVES OF METHIONINE FOR GROWTH PURPOSES

INTRODUCTION

Methionine and cystine are the only known sulfur-containing amino acids of proteins. Womack, Kemmerer, and Rose¹ have shown that methionine is an indispensable amino acid for the immature rat by feeding diets containing highly purified amino acids as the nitrogen source. They also proved that cystine is incapable of promoting growth when methionine is absent from the food.

It is possible to use the method of growth as an index to the effectiveness with which a compound may be substituted in the diet for an indispensable amino acid. The alpha-keto² and the alpha-hydroxy³ analogues of methionine have been found capable of this replacement. The aim of the present investigation was to determine the availability of the following

derivatives of methionine for the purpose of growth in the rat: acetyl-, benzoyl-, carbamyl-dl-methionine, the diketopiperazine, pseudomethionine, and the hydantoin corresponding to this amino acid.

EXPERIMENTAL

Albino rats weighing 45 to 60 gm. each received diets which were devoid of protein but contained a mixture of highly purified amino acids. In separate tests, methionine of the ration was replaced by the synthetic compounds in question. The growth rate of the animals was compared to that of positive controls receiving methionine. Each test was continued for twenty-eight days.

SUMMARY

By the method of growth as an index of physiological availability, it has been shown that acetyl-dl-methionine can serve in place of the free amino acid. Inclusion in the diet of either benzoyl-dl-methionine, carbamyl-dl-methionine, the hydantoin, the diketopiperazine, or pseudomethionine is totally without effect upon the body weight losses resulting from a methionine deficiency.

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PART III

THE INABILITY OF BETA-HYDROXYLEUCINE TO REPLACE LEUCINE IN THE DIET

INTRODUCTION

It is possible to use the method of growth to determine from what precursors the animal is able to synthesize necessary dietary components. In unpublished experiments¹ in

this laboratory it has been shown that d-threo- β,γ -dihydroxy- α -aminobutyric acid is totally incapable of replacing threonine. Furthermore, the compound is highly toxic and leads to the death of the animals. For this reason, β -hydroxyleucine was prepared and tested for its ability to replace the leucine in the diet.

EXPERIMENTAL

Albino rats weighing 45 to 60 gms. each served as the experimental animals. The diets were devoid of protein but contained mixtures of highly purified amino acids. The leucine of the ration was replaced by β -hydroxyleucine. The growth rate was compared with positive controls receiving leucine. The feeding experiments were continued until the subjects succumbed.

SUMMARY

Feeding experiments involving the use of diets containing mixtures of highly purified amino acids have shown that β -hydroxyleucine is totally incapable of replacing leucine for purposes of growth. Furthermore, the compound is highly toxic and causes the death of the subjects promptly.

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PART IV

THE QUANTITATIVE REQUIREMENT FOR PHENYLALANINE IN MAN

INTRODUCTION

Nitrogen equilibrium studies have been used to determine which of the amino acids are indispensable for the human^{1,2,3}. The results of these studies showed that eight of the ten amino acids previously found to be essential for the rat are indispensable for man. Histidine² and arginine³ are not necessary for the maintenance of nitrogen balance in human

subjects. The present study was carried out to determine the minimum amount of phenylalanine which is necessary for maintenance of nitrogen balance.

EXPERIMENTAL

Three adult male subjects were used in this experiment. Rations were fed in which more than ninety-five per cent of the nitrogen was in the form of highly purified amino acids. In addition to the amino acid mixture the diets contained butter, starch, sucrose, lemon juice, cellu-flour, corn oil, cod liver oil, minerals, and a mixture of vitamins. Distilled water was taken *ad libitum*.

Twenty-four hour urine samples were collected and preserved under toluene. Fecal periods were marked off with charcoal tablets. The level of nitrogen was kept constant at 9.99 gm. per day. The subjects were maintained in nitrogen equilibrium for at least four days before the phenylalanine content of the diet was altered. The quantity of this amino acid was then diminished until each subject showed a definite state of negative balance for at least four days. The minimum requirement was determined to the nearest 0.2 gram of phenylalanine.

SUMMARY

By using the principle of nitrogen equilibrium, the quantitative requirement for phenylalanine has been determined for three human subjects.

The findings were quite variable but indicate that the daily intake of this amino acid need not exceed 1.87 gm. for a 70 kilogram man.

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VITA

The author was born April 5, 1915 in Center, Mississippi. He received his elementary and secondary education in the public schools of central Mississippi. He attended Mississippi State College from which he received his Bachelor of Science Degree in June, 1938. He entered the graduate school of the Virginia Polytechnic Institute, Blacksburg, Virginia, in September, 1938 and served as a Research Fellow in Chemistry. He received the Master of Science Degree from the latter institution in June, 1939. The following two years were spent as a Research Assistant in the Biochemistry Department of the Medical College of Virginia, Richmond, Virginia. He entered the graduate school of the University of Illinois in September, 1941 as a Special Research Assistant in Chemistry, holding this appointment for the succeeding two years. During the summer semester of 1943 he was a teaching assistant for the Army Specialized Training Program. In October, 1943 he received an appointment as special research assistant under a grant from the Nutrition Foundation.



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